CLAIMS

1. A method for treating a vascular hyperpermeable disease (except macular edema), which method comprises administering to a subject in need thereof a vascular adhesion protein-1 (VAP-1) inhibitor in an amount sufficient to treat said subject for said disease.

2. The method of claim 1, wherein said disease is a disease in mucous membrane.

3. The method of claim 2, wherein said mucous membrane is a mucous membrane of ocular, cutis, otorhinology or respiratory tract.

4. The method of claim 1, wherein said disease is aged macular degeneration, aged disciform macular degeneration, cystoid macular edema, palpebral edema, retinal edema, diabetic retinopathy, chorioretinopathy, neovascular maculopathy, neovascular glaucoma, uveitis, iritis, retinal vasculitis, endophthalmitis, panophthalmitis, metastatic ophthalmia, choroiditis, retinal pigment epithelitis, conjunctivitis, cyclitis, scleritis, episcleritis, optic neuritis, retrobulbar optic neuritis, keratitis, blepharitis, exudative retinal detachment, corneal ulcer, conjunctival ulcer, chronic nummular keratitis, Thygeson keratitis, progressive Mooren's ulcer, an ocular inflammatory disease caused by bacterial or viral infection, and by an ophthalmic operation, an ocular inflammatory disease caused by a physical injury to the eye, a symptom caused by an ocular inflammatory disease including itching, flare, edema and ulcer, erythema, erythema exsudativum multiforme, erythema nodosum, erythema annulare, scleredema, dermatitis,

angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

5. The method of claim 1, wherein the VAP-1 inhibitor is a compound of the formula (I):

$$R^1—NH—X—Y—Z \quad (I)$$

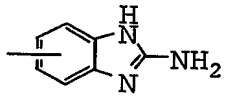
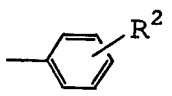
wherein

R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or -CONH-; and

Z is a group of the formula:

 or 

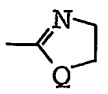
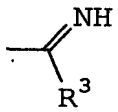
wherein R^2 is a group of the formula: -A-B-D-E

wherein A is a bond, lower alkylene, -NH- or $-SO_2-$;

B is a bond, lower alkylene, -CO- or -O-;

D is a bond, lower alkylene, -NH- or $-CH_2NH-$; and

E is optionally protected amino, $-N=CH_2$,

 or 

wherein

Q is -S- or -NH-; and

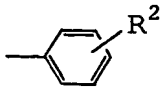
R^3 is hydrogen, lower alkyl, lower alkylthio or $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

or a derivative thereof;

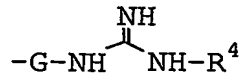
or a pharmaceutically acceptable salt thereof.

6. The method of claim 5, wherein, in the formula (I), Z is a

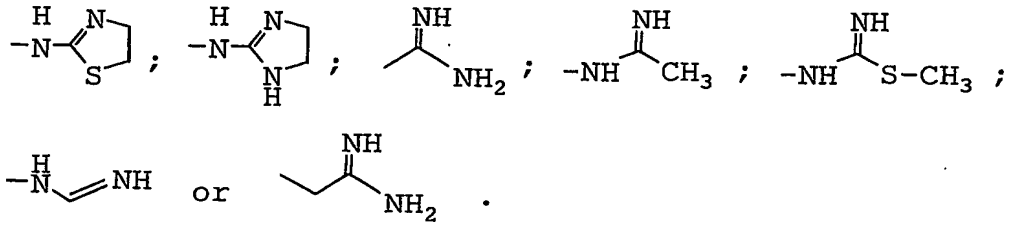
group of the formula:



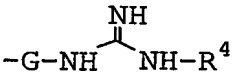
wherein R^2 is a group of the formula:



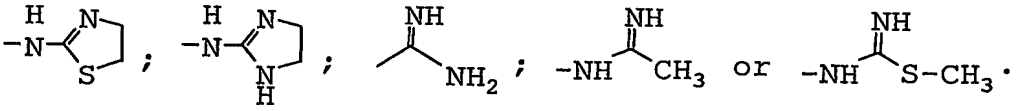
(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen, $-NH_2$ or lower alkyl); $-NH_2$; $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



7. The method of claim 6, wherein, in the formula (I), R^2 is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



8. The method of any of claims 5 to 7, wherein, in the formula (I), R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl.

9. The method of claim 1, wherein the VAP-1 inhibitor is N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,

N-[4-(2-{4-[(aminooxy)methyl]phenyl}ethyl)-1,3-thiazol-2-yl]acetamide,

N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or

N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

10. The method of claim 1, wherein the VAP-1 inhibitor is N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition for the treatment of a vascular hyperpermeable disease (except macular edema), which comprises, as an active ingredient, a VAP-1 inhibitor.

12. The composition of claim 11, wherein said disease is a disease in mucous membrane.

13. The composition of claim 12, wherein said mucous membrane is a mucous membrane of ocular, cutis, otorhinology or respiratory tract.

14. The composition of claim 11, wherein said disease is aged macular degeneration, aged disciform macular degeneration, cystoid macular edema, palpebral edema, retinal edema,

diabetic retinopathy, chorioretinopathy, neovascular maculopathy, neovascular glaucoma, uveitis, iritis, retinal vasculitis, endophthalmitis, panophthalmitis, metastatic ophthalmia, choroiditis, retinal pigment epithelitis, conjunctivitis, cyclitis, scleritis, episcleritis, optic neuritis, retrobulbar optic neuritis, keratitis, blepharitis, exudative retinal detachment, corneal ulcer, conjunctival ulcer, chronic nummular keratitis, Thygeson keratitis, progressive Mooren's ulcer, an ocular inflammatory disease caused by bacterial or viral infection, and by an ophthalmic operation, an ocular inflammatory disease caused by a physical injury to the eye, a symptom caused by an ocular inflammatory disease including itching, flare, edema and ulcer, erythema, erythema exsudativum multiforme, erythema nodosum, erythema annulare, scleredema, dermatitis, angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

15. The composition of claim 11, wherein the VAP-1 inhibitor is a compound of the formula (I):

$$R^1—NH—X—Y—Z \quad (I)$$

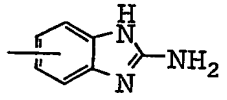
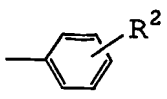
wherein

R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or -CONH-; and

Z is a group of the formula:

 or 

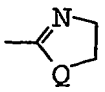
wherein R^2 is a group of the formula: -A-B-D-E

wherein A is a bond, lower alkylene, -NH- or $-SO_2-$;

B is a bond, lower alkylene, -CO- or -O-;

D is a bond, lower alkylene, -NH- or $-CH_2NH-$; and

E is optionally protected amino, $-N=CH_2$,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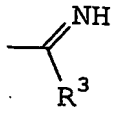


wherein

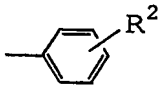
Q is -S- or -NH-; and

R^3 is hydrogen, lower alkyl, lower alkylthio or $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

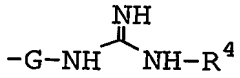
or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

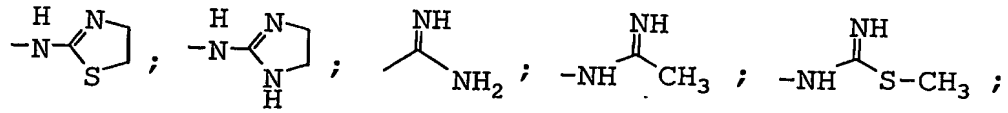
16. The composition of claim 15, wherein, in the formula (I), Z is a group of the formula:

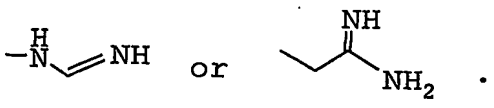


wherein R^2 is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen, $-NH_2$ or lower alkyl); $-NH_2$; $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;




or

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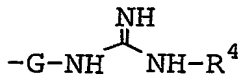
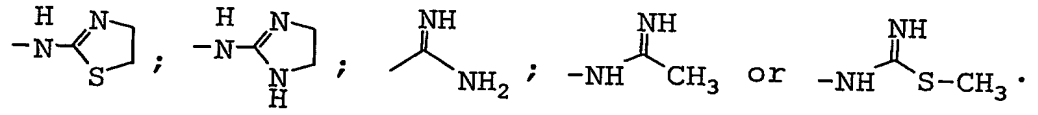
17. The composition of claim 16, wherein, in the formula (I), R^2 is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



18. The composition of any of claims 15 to 17, wherein, in the formula (I), R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl.

19. The composition of claim 11, wherein the VAP-1 inhibitor is

N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,

N-[4-(2-{4-[(aminooxy)methyl]phenyl}ethyl)-1,3-thiazol-2-yl]acetamide,

N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or

N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

20. The composition of claim 11, wherein the VAP-1 inhibitor is

N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-

thiazol-2-yl}acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

21. A use of a VAP-1 inhibitor for preparing a medicament for the treatment of a vascular hyperpermeable disease (except macular edema).

22. The use of claim 21, wherein said disease is a disease in mucous membrane.

23. The use of claim 22, wherein said mucous membrane is a mucous membrane of ocular, cutis, otorhinology or respiratory tract.

24. The use of claim 21, wherein said disease is aged macular degeneration, aged disciform macular degeneration, cystoid macular edema, palpebral edema, retinal edema, diabetic retinopathy, chorioretinopathy, neovascular maculopathy, neovascular glaucoma, uveitis, iritis, retinal vasculitis, endophthalmitis, panophthalmitis, metastatic ophthalmia, choroiditis, retinal pigment epithelitis, conjunctivitis, cyclitis, scleritis, episcleritis, optic neuritis, retrobulbar optic neuritis, keratitis, blepharitis, exudative retinal detachment, corneal ulcer, conjunctival ulcer, chronic nummular keratitis, Thygeson keratitis, progressive Mooren's ulcer, an ocular inflammatory disease caused by bacterial or viral infection, and by an ophthalmic operation, an ocular inflammatory disease caused by a physical injury to the eye, a symptom caused by an ocular inflammatory disease including itching, flare, edema and ulcer, erythema, erythema exsudativum multiforme, erythema nodosum, erythema annulare, scleredema, dermatitis,

angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

25. The use of claim 21, wherein the VAP-1 inhibitor is a compound of the formula (I):

$$R^1—NH—X—Y—Z \quad (I)$$

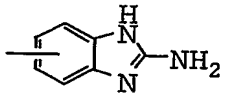
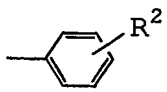
wherein

R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or -CONH-; and

Z is a group of the formula:

 or 

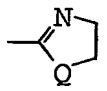
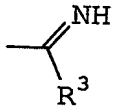
wherein R^2 is a group of the formula: -A-B-D-E

wherein A is a bond, lower alkylene, -NH- or $-SO_2-$;

B is a bond, lower alkylene, -CO- or -O-;

D is a bond, lower alkylene, -NH- or $-CH_2NH-$; and

E is optionally protected amino, $-N=CH_2$,

 or 

wherein

Q is -S- or -NH-; and

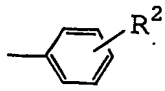
R^3 is hydrogen, lower alkyl, lower alkylthio or $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

or a derivative thereof;

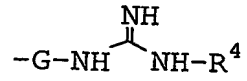
or a pharmaceutically acceptable salt thereof.

26. The use of claim 25, wherein, in the formula (I), Z is a

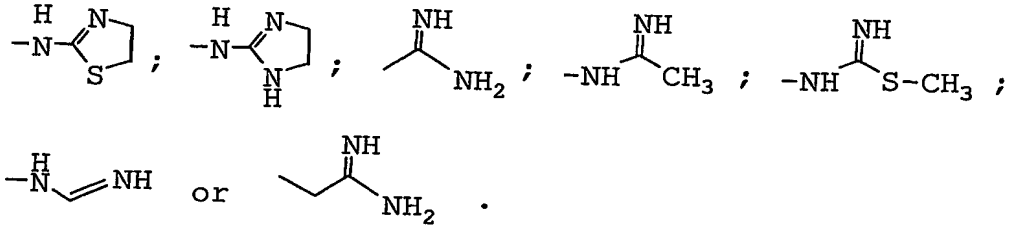
group of the formula:



wherein R^2 is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen, $-NH_2$ or lower alkyl); $-NH_2$; $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



28. The use of any of claims 25 to 27, wherein, in the formula (I), R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl.

29. The use of claim 21, wherein the VAP-1 inhibitor is N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide,

N-[4-(2-{4-[(aminooxy)methyl]phenyl}ethyl)-1,3-thiazol-2-

yl]acetamide,

N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl}acetamide,

N-{4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide, or

N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

30. The use of claim 21, wherein the VAP-1 inhibitor is N-{4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl}acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.